M 1023N

HFI-35

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUN 25 1997

WARNING LETTER

VIA FEDERAL EXPRESS

Ms. Elizabeth Fothergill
Managing Director
Ivor Shaw/Pennine Healthcare Ltd.
Pontefract Street
Ascot Drive
Derby DE24 8JD, United Kingdom

Dear Ms. Fothergill:

During an inspection of your firm located at Derby in the United Kingdom, on February 17 through 20, 1997, our investigator determined that your firm manufactures suction catheters, urinary catheters, and tubing. These products are devices as defined by Section 201(h) of the Federal Food, Drug and Cosmetic Act (the Act).

The above stated inspection revealed that these devices are adulterated within the meaning of Section 501(h) of the Act, in that the methods used in, or the facilities or controls used for their manufacture, packing, storage, or installation are not in conformity with the Good Manufacturing Practice (GMP) for Medical Devices Regulation, as specified in Title 21, Code of Federal Regulations (CFR), Part 820, as follows:

1. Failure to establish and implement specification control measures to assure that the design basis for the device and packaging is correctly translated into approved specifications, as required by 21 CFR 820.100(a)(1). For example:

   a. [redacted] processes have not been validated.

   Your response is not adequate because it does not give evidence of, or propose validation of the processes performed on the [redacted] Your response indicates that "manufacturing process validation is an integral part of the design control process" and that in Europe retrospective design control is not required. The response appears to confuse design validation with process validation. The validation of a manufacturing process is not an element of design control; nor is it a new requirement. Process validation has long been considered an important aspect of compliance with the 1978 GMP regulation (21 CFR 820).

Your response asserts that process validation is not necessary for establishing machine settings for [redacted] machines because the settings "have been established historically." However, the historical data was not submitted correlating settings for specific runs with quantitative results for those runs. The response does not address validation of the [redacted] processes.

We note that this charge was also included on the FDA 483 issued at the conclusion of the previous inspection in 1995.

b. Procedures for Process Validation [redacted] do not include provisions requiring a written plan before beginning a validation study.

Your response is not adequate because it did not provide for the preparation of a written plan, or protocol, defining the process validation studies.

2. Failure to design and construct the device package to protect the device from alteration or damage during the customary conditions of processing, storage, handling, and distribution, as required by 21 CFR 820.130. For example, there is no inspection of the device pouches following sterilization.

Your response is not adequate because no evidence was provided to show that device pouches are inspected following sterilization or that process validation studies have adequately demonstrated that the sterilization process does not adversely affect the pouch integrity. We note that this charge was also included on the FDA 483 issued at the conclusion of the previous inspection in 1995.

3. Failure to have a device master record which includes production process specifications including the appropriate equipment specifications, production methods, production procedures, and production environment specifications, as required by 21 CFR 820.181(b). For example, the written procedures, [redacted], do not include employee instructions for machine set-up and operation.

Your response is not adequate because amended instructions were not submitted to demonstrate that instructions are now complete.

Although we have not included observation 4 of the FDA 483 in the list of deficiencies, we will answer the question that you raised in your response regarding the applicability of the regulation to the type of complaint addressed during the inspection. You referenced the FDA response number 14 in the preamble, dated October 7, 1997, to the Quality System regulation. Although this regulation had not been implemented at the time of the inspection, the question raised here is also applicable to the GMP regulation of 1978. The requirements of the GMP regulation do apply to this complaint because the regulation (and the preamble comments) state that when a customer communication regards the "identity" of a device after it is released for distribution, then the communication is considered to be a complaint. In this case, the customer complained about a shipment that apparently included misidentified product. The customer asked for assistance in identifying which lot numbers were made to each product number specification. Therefore, the GMP regulation required that this incident be treated as a complaint within your complaint handling system.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the FDA 483 issued at the close-out of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the Food and Drug Administration. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

We acknowledge that you have submitted responses dated February 25, 1997, and April 14, 1997, concerning our investigator's observations noted on the form FDA 483. As discussed in the enclosed review, your response does not adequately address those violations relating to process validation, post-sterilization inspection of device pouches, and employee instructions for machine set-up and operation.

Other federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts.

Given the serious nature of these violations of the Act, all sterile devices manufactured by Ivor Shaw/Pennine Healthcare Ltd., Pontefract Street, Ascot Drive, Derby DE24 8JD, United Kingdom may be detained without physical examination upon entry into the United States (U.S.) until these violations are corrected.

In order to remove the sterile devices from this detention, it will necessary for you to provide a written response to the charges in this Warning Letter for our review. After we notify you that the response is adequate, it will be your responsibility to schedule an inspection of your facility. As soon as the inspection has taken place, and the implementation of your corrections has been verified, your products may resume entry into this country. This detention does not include non-sterile devices.

Please notify this office in writing of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to identify and make corrections to any underlying systems problems necessary to assure that similar violations will not recur. Please include any and all documentation to show that adequate correction has been achieved. In the case of future corrections, an estimated date of completion, and documentation showing plans for correction, should be included with your response to this letter.

Please address your response to:

George Kroehling, Chief
General Surgery Devices Branch
Division of Enforcement I
Office of Compliance
Center for Devices and Radiological Health
2098 Gaither Road
Rockville, MD 20850
USA

If you have any questions, please contact Sarah Mowitt at the above address. If you need assistance, contact Mrs. Mowitt by phone at (301) 594-4595 or by FAX (301) 594-4636.

Sincerely yours,

Lillian J. Gill
Director
Office of Compliance
Center for Devices and
Radiological Health